Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 21 January, 2010. Claims 1-11 and 13-23 are pending in the instant application. New claims 22 and 23 accompanied the response. Claims 1-11, 13-17, 22, and 23 are currently under examination while claims 18-21 stand withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 C.F.R. § 1.144). See M.P.E.P. § 821.01.

37 C.F.R. § 1.84

Acknowledgement is hereby made of receipt and entry of the drawings filed on 21 January, 2010, which are deemed to be acceptable.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 1-11, 13-17, and 22 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant, is hereby withdrawn in response to applicants' amendment and arguments.

Claim 23 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claim references a "modified" HIV-1 gp41 polypeptide comprising a linker that replaces amino acids 593-617. First, the precise amino acid sequence of this peptide is not readily manifest. The disclosure describes the preparation of modified HIV-1 gp41 polypeptides comprising an IDR, N-helix, C-helix, and synthetic hydrophilic linker wherein said modified polypeptide maintains its native configuration while also providing a soluble and stable form. However, no such limitations appear in this particular claim. It is not readily manifest if the claims are simply directed toward a modified gp41 comprising the linker, or if other modifications are present. Second, it is not readily manifest what purpose this linker serves. Applicants may wish to amend the preamble to incorporate suitable functional limitations (e.g., A modified

HIV-1 gp41 polypeptide with increased solubility as compared to the wildtype gp41 comprising...). Finally, the claim lacks sufficient antecedent basis for the limitation "the linker" in the claim. Appropriate correction is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

Claims 1 and 9-11 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The amended claims are directed toward a modified polypeptide comprising an immunodominant region, N-helix, C-helix, and linker. It was further stipulated that additional modifications are present that eliminate or reduce autoimmune responses against a host protein. Appropriately drafted claim language directed toward the modified polypeptides of SEQ ID NOS. 8, 17, 18, 19, 20, and 21 would be acceptable.

As previously set forth, the legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d

1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide sufficient guidance pertaining to suitable mutations that prevent cross-reactivity with host B- or T-cell epitopes (see claims 9 and 10). The disclosure fails to identify suitable cross-reactive epitopes present in the modified polypeptide and it fails to identify suitable mutations that will abrogate immunological cross-reactivity while maintaining the desirable polypeptide properties.

2) The claim breadth is considerable and encompasses a large number of mutants comprising amino acid substitutions, additions, and deletions. However, the disclosure fails to provide a detailed structural/functional analysis of polypeptide mutants that retain the desired properties.

3) The disclosure fails to provide a sufficient number of working embodiments. Considering the unpredictability associated with mutagenic studies, multiple working examples would be

required to enable the full breadth of the patent protection desired.

4) The state-of-the-art teaches that single amino acid additions, deletions, or substitutions can abrogate polypeptide activity (i.e., antigen-antibody binding interactions). Thus considerable guidance would be required from the specification identifying suitable mutants.

When all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the invention in a manner commensurate in scope with the claims. Applicants may obviate the rejection by amending the claim language as suggested *supra*.

Applicants argue the amended claims are fully supported by the disclosure. These arguments are clearly not persuasive. The claims fail to identify any suitable autoimmune epitopes and appropriate modifications that will lead to a peptide with the desired properties. Moreover, as previously noted, the disclosure fails to provide a reasonable number of mutant polypeptides with the recited properties. Accordingly the rejection is proper and hereby maintained.

Enablement

The previous rejection of claim 22 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is hereby withdrawn in response to applicant's amendment.

New Matter

Claims 1-11, 13-17, 22, and 23 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). The amended claims introduce new limitations pertaining to the region within gp41 that accommodates the hydrophilic linker (e.g., amino acids 599-610 or 593-617). Perusal of the disclosure failed to identify precise support for these limitations. The disclosure clearly identifies preferred insertion regions. For example, Figure 2 discloses various regions of interest (amino acids 590-620, 598-622, etc.). The specification also discusses various insertion points (see p. 4, lines 4-8). However, the precise regions currently claimed could not be identified. Applicants are invited to identify those regions of the disclosure that provide support for the claimed limitations.

Allowable Subject Matter

The modified HIV-1 gp41 polypeptides corresponding to SEQ ID NOS.: 8 and 17-21 appear to be free of the prior art. Amendment of the claim language as suggested *supra* would facilitate the allowance process.

Action Is Final

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing

date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

26 April, 2010